Clinical trial results:
Albiglutide + Insulin Glargine Versus Insulin Lispro + Insulin Glargine in the Treatment of Subjects With Type 2 Diabetes Mellitus: The Switch Study

Summary

EudraCT number	2014-001821-34
Trial protocol	HU DE IT ES GB PL
Global end of trial date	24 July 2017

Results information

Result version number	v1 (current)
This version publication date	17 June 2018
First version publication date	17 June 2018

Trial information

Trial identification

Sponsor protocol code	200977

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	21 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the glycemic effectiveness of once-weekly albiglutide as replacement of prandial insulin in participants with T2DM receiving basal-bolus insulin therapy.

Protection of trial subjects:

An insulin titration surveillance process was conducted on an ongoing basis to provide medical surveillance of subject's insulin titration per the titration recommended algorithm specified in the protocol with diligent medical oversight for events of hypoglycemia and glucose readings meeting specific criteria.
Additionally, there was a defined email alert process in place to identify blood glucose readings reported from participant eDiary uploads which were <=50 milligrams/deciliter (mg/dL) or >=270 mg/dL. Email alerts triggered a follow-up communication with the site to ensure appropriate patient management.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 November 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 20
Country: Number of subjects enrolled	United States: 125
Country: Number of subjects enrolled	Mexico: 166
Country: Number of subjects enrolled	Brazil: 150
Country: Number of subjects enrolled	Hungary: 69
Country: Number of subjects enrolled	Poland: 74
Country: Number of subjects enrolled	France: 11
Country: Number of subjects enrolled	Germany: 73
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Spain: 46
Country: Number of subjects enrolled	United Kingdom: 6
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Philippines: 28
Country: Number of subjects enrolled	South Africa: 17
Worldwide total number of subjects	814
EEA total number of subjects	301

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	601
From 65 to 84 years	213
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted from 21-Nov-2014 to 24-Jul-2017 at 186 centers in 14 countries: Canada, United States of America, Mexico, Brazil, Hungary, Poland, France, Germany, Italy, Spain, United Kingdom, Korea, Philippines and South Africa.

Pre-assignment

Screening details:

A total of 2004 participants were screened, of which 973 participants were screen failures and 160 participants were re-screened. A total of 1031 participants then entered the standardization period, of which 217 participants were standardization failures. A total of 814 participants were randomized in the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Albiglutide + Insulin Glargine

Arm description:

During standardization period, participants transitioned from basal bolus regimen received during screening period to insulin glargine plus insulin lispro. Eligible participants received Albiglutide 30 milligrams (mg) weekly subcutaneous (SC) injection during the treatment period and insulin lispro dose was down-titrated to half that used in the standardization period. At Week 4, Albiglutide was up-titrated to 50 mg weekly SC injection and insulin lispro was stopped for the remainder of the treatment period.

Arm type	Experimental
Investigational medicinal product name	Albiglutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Albiglutide was intended for self-administration as a SC injection. It was provided as a fixed dose of 30 mg of albiglutide or 50 mg of albiglutide in a 0.5 milliliters (mL) injection volume, fully disposable pen injector.

Investigational medicinal product name	Insulin Glargine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin glargine was provided as injection pen for SC injection.

Arm title	Insulin Lispro + Insulin Glargine

Arm description:

During standardization period, participants transitioned from basal bolus regimen received during screening period to insulin glargine plus insulin lispro. Eligible participants continued with the same doses as at the end of the standardization period and doses were adjusted according to protocol-defined insulin titration algorithms. Participants received Insulin Glargine along with Insulin Lispro during the treatment period.

Arm type	Experimental

Investigational medicinal product name	Insulin Glargine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin glargine was provided as injection pen for SC injection.

Investigational medicinal product name	Insulin Lispro
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

Insulin lispro was provided as injection pen for SC injection.

Number of subjects in period 1	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine
Started	402	412
Completed	351	350
Not completed	51	62
Adverse event, serious fatal	-	1
Consent withdrawn by subject	8	12
Physician decision	5	12
Adverse event, non-fatal	14	8
Protocol defined stopping criteria	1	3
Unknown	-	1
Study terminated by sponsor	11	11
Lost to follow-up	3	3
Lack of efficacy	3	3
Protocol deviation	6	8

Baseline characteristics

Reporting groups	
Reporting group title	Albiglutide + Insulin Glargine
Reporting group description:	
During standardization period, participants transitioned from basal bolus regimen received during screening period to insulin glargine plus insulin lispro. Eligible participants received Albiglutide 30 milligrams (mg) weekly subcutaneous (SC) injection during the treatment period and insulin lispro dose was down-titrated to half that used in the standardization period. At Week 4, Albiglutide was up-titrated to 50 mg weekly SC injection and insulin lispro was stopped for the remainder of the treatment period.	
Reporting group title	Insulin Lispro + Insulin Glargine
Reporting group description:	
During standardization period, participants transitioned from basal bolus regimen received during screening period to insulin glargine plus insulin lispro. Eligible participants continued with the same doses as at the end of the standardization period and doses were adjusted according to protocol-defined insulin titration algorithms. Participants received Insulin Glargine along with Insulin Lispro during the treatment period.	

Reporting group values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine	Total
Number of subjects	402	412	814
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	58.0	58.1	
standard deviation	± 9.40	± 9.49	-
Gender categorical Units: Subjects			
Female	228	214	442
Male	174	198	372
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	43	28	71
Asian-Central/South Asian (A) Heritage (H)	5	8	13
Asian-Japanese H/East AH/South East AH	25	24	49
Black or African American	37	32	69
Native Hawaiian or Other Pacific Islander	1	3	4
White	284	312	596
Multiple-Black or African American and White	7	5	12

End points

End points reporting groups

Reporting group title	Albiglutide + Insulin Glargine

Reporting group description:

During standardization period, participants transitioned from basal bolus regimen received during screening period to insulin glargine plus insulin lispro. Eligible participants received Albiglutide 30 milligrams (mg) weekly subcutaneous (SC) injection during the treatment period and insulin lispro dose was down-titrated to half that used in the standardization period. At Week 4, Albiglutide was up-titrated to 50 mg weekly SC injection and insulin lispro was stopped for the remainder of the treatment period.

Reporting group title	Insulin Lispro + Insulin Glargine

Reporting group description:

During standardization period, participants transitioned from basal bolus regimen received during screening period to insulin glargine plus insulin lispro. Eligible participants continued with the same doses as at the end of the standardization period and doses were adjusted according to protocol-defined insulin titration algorithms. Participants received Insulin Glargine along with Insulin Lispro during the treatment period.

Subject analysis set title	Albiglutide + Insulin Glargine
Subject analysis set type	Safety analysis

Subject analysis set description:

During standardization period, participants transitioned from basal bolus regimen received during screening period to insulin glargine plus insulin lispro. Eligible participants received Albiglutide 30 mg weekly SC injection during the treatment period and insulin lispro dose was down-titrated to half that used in the standardization period. At Week 4, Albiglutide was up-titrated to 50 mg weekly SC injection and insulin lispro was stopped for the remainder of the treatment period.

Subject analysis set title	Insulin Lispro + Insulin Glargine
Subject analysis set type	Safety analysis

Subject analysis set description:

During standardization period, participants transitioned from basal bolus regimen received during screening period to insulin glargine plus insulin lispro. Eligible participants continued with the same doses as at the end of the standardization period and doses were adjusted according to protocol-defined insulin titration algorithms. Participants received Insulin Glargine along with Insulin Lispro during the treatment period.

Primary: Change from Baseline in glycosylated hemoglobin (HbA1c) at Week 26

End point title	Change from Baseline in glycosylated hemoglobin (HbA1c) at Week 26

End point description:

HbA1c is glycosylated hemoglobin. It was measured at Baseline and at Week 26. The analysis was conducted using mixed-effect model with repeated measures (MMRM). The model included HbA1c change from Baseline as the dependent variable; treatment, region, age category, current metformin use, visit week, treatment-by-week interaction, and Baseline HbA1c-by-week interaction as fixed effects; Baseline HbA1c as a continuous covariate; and participant as a random effect. The Baseline value was the last available non-missing value prior to the first dose of the randomized treatment, thus Baseline was Day -1. Change from Baseline is defined as the post-Baseline value minus the Baseline value. Full Analysis (FA) Population comprised of all participants who were randomly assigned to treatment (who did not receive any study treatment were also included). Only those participants available at the specified time points were analyzed.

End point type	Primary

End point timeframe:

Baseline (Day -1) and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	345[1]	350[2]		
Units: Percentage of glycosylated hemoglobin				
least squares mean (standard error)				
Percentage of glycosylated hemoglobin	-1.04 (± 0.041)	-1.10 (± 0.040)		

Notes:

[1] - FA Population. Only those participants available at the specified time points were analyzed.

[2] - FA Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Least Square mean of albiglutide + insulin glargine from insulin lispro + insulin glargine has been presented.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	695
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.0001 [4]
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.17

Notes:

[3] - If the upper bound of the confidence interval is less than or equal to 0.3%, non-inferiority will be concluded.

[4] - Non-inferiority p-value. P-value from testing the null hypothesis that the difference in change from baseline least squares means (albiglutide-insulin lispro) is greater than 0.30% based on one-sided t-test with 0.025 level of significance.

Secondary: Number of participants treated with once-weekly albiglutide that were able to discontinue insulin lispro at Week 4 and did not meet prespecified criteria for severe, persistent hyperglycemia through Week 26

End point title	Number of participants treated with once-weekly albiglutide that were able to discontinue insulin lispro at Week 4 and did not meet prespecified criteria for severe, persistent hyperglycemia through Week 26[5]

End point description:

Participants who did not meet prespecified criteria for severe, persistent hyperglycemia through Week 26 were those participants treated with once-weekly albiglutide that were able to replace prandial insulin without lispro re-introduction through Week 26. Number of participants treated with once-weekly albiglutide that were able to discontinue insulin lispro at Week 4 and did not meet prespecified criteria for severe, persistent hyperglycemia through Week 26 have been presented.

End point type	Secondary

End point timeframe:

Up to Week 26

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Since the endpoint is about participants treated with Albiglutide, data has been provided for the single arm containing Albiglutide.

End point values	Albiglutide + Insulin Glargine			
Subject group type	Reporting group			
Number of subjects analysed	402[6]			
Units: Participants				
Participants	218			

Notes:

[6] - FA Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with severe or documented symptomatic hypoglycemia through Week 26

End point title	Percentage of participants with severe or documented symptomatic hypoglycemia through Week 26

End point description:

Severe hypoglycemia was considered as an event requiring assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions. Plasma glucose concentrations may not be available during an event, but neurological recovery following the return of plasma glucose to normal was considered sufficient evidence that the event was induced by a low plasma glucose concentration. Documented symptomatic hypoglycemia was an event during which typical symptoms of hypoglycemia are accompanied by a measured plasma glucose concentration <=70 milligrams per deciliters (mg/dL) (<=3.9 millimoles per liters [mmol/L]).

End point type	Secondary

End point timeframe:

Up to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[7]	412[8]		
Units: Percentage of participants				
number (not applicable)				
Percentage of participants	57.2	75.0		

Notes:

[7] - FA Population. Only those participants available at the specified time points were analyzed.

[8] - FA Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [9]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	0.6

Notes:

[9] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for Baseline HbA1c category, age category, region and current use of metformin.

Secondary: Change from Baseline in body weight at Week 26

End point title	Change from Baseline in body weight at Week 26

End point description:

Body weight was measured to the nearest 0.1 kilogram on a standard calibrated scale. Participants dressed in light indoor clothes (no coat, jacket, etc.) without shoes and with a voided bladder. The same equipment was used wherever possible. The Baseline value was the last available non-missing value prior to the first dose of the randomized treatment, thus Baseline was Day -1. Change from Baseline is defined as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	349[10]	352[11]		
Units: Kilograms				
least squares mean (standard error)				
Kilograms	-1.95 (± 0.207)	2.43 (± 0.205)		

Notes:

[10] - FA Population. Only those participants available at the specified time points were analyzed.

[11] - FA Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Least Square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine

Number of subjects included in analysis	701
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-4.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.93
upper limit	-3.82

Secondary: Change from Baseline to Week 26 in body weight

End point title	Change from Baseline to Week 26 in body weight

End point description:

Body weight was measured to the nearest 0.1 kilogram on a standard calibrated scale. Participants dressed in light indoor clothes (no coat, jacket, etc.) without shoes and with a voided bladder. The same equipment was used wherever possible. The Baseline value was the last available non-missing value prior to the first dose of the randomized treatment, thus Baseline was Day -1. Change from Baseline is defined as the post-Baseline value minus the Baseline value. Change from Baseline to Week 26 in body weight are presented. FA Population was analyzed. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles.

End point type	Secondary

End point timeframe:

Baseline (Day -1) to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[12]	412[13]		
Units: Kilograms				
least squares mean (standard error)				
Week 4, n=368,384	-0.55 (± 0.091)	0.66 (± 0.091)		
Week 5, n=382,393	-0.95 (± 0.102)	0.85 (± 0.102)		
Week 10, n=379,397	-1.71 (± 0.133)	1.46 (± 0.131)		
Week 18, n=365,372	-1.96 (± 0.177)	2.06 (± 0.175)		
Week 26, n=349,352	-1.95 (± 0.207)	2.43 (± 0.205)		

Notes:

[12] - FA Population.

[13] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Least Square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) at Week 4 has been presented.	
Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.43
upper limit	-1

Statistical analysis title	Statistical analysis 2
Statistical analysis description: Least Square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) at Week 5 has been presented.	
Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.05
upper limit	-1.55

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Least Square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) at Week 10 has been presented.	
Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-3.17

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.51
upper limit	-2.82

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Least Square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) at Week 18 has been presented.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-4.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.48
upper limit	-3.54

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Least Square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) at Week 26 has been presented.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-4.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.93
upper limit	-3.82

Secondary: Total daily insulin dose at Week 26

End point title	Total daily insulin dose at Week 26

End point description:

Insulin dose at Week 26 was defined as the prescribed insulin dose at Week 25. Based on mixed model repeated measure (MMRM) model, prescribed total daily basal insulin dose was equal to Baseline prescribed total daily basal insulin dose + treatment + Baseline HbA1c category + region + age category + current use of metformin + visit week + treatment-by-visit week interaction + Baseline prescribed total daily basal insulin dose-by-visit week interaction. Total daily insulin dose at Week 26 is presented. Only those participants available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	342[14]	341[15]		
Units: International Units				
least squares mean (standard error)				
International Units	70.36 (± 2.160)	131.19 (± 2.149)		

Notes:

[14] - FA Population. Only those participants available at the specified time points were analyzed.

[15] - FA Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	683
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-60.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.57
upper limit	-55.1

Secondary: Change from Baseline to Week 26 in HbA1c

End point title	Change from Baseline to Week 26 in HbA1c

End point description:

HbA1c is glycosylated hemoglobin and was measured up to Week 26. The Baseline value was the last available non-missing value prior to the first dose of the randomized treatment, thus Baseline was Day

-1. Change from Baseline is defined as the post-Baseline value minus the Baseline value. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles.

End point type	Secondary

End point timeframe:

Baseline to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[16]	412[17]		
Units: Percentage of glycosylated hemoglobin				
least squares mean (standard error)				
Week 4, n=358,375	-0.59 (± 0.023)	-0.47 (± 0.023)		
Week 5, n=374,392	-0.67 (± 0.026)	-0.58 (± 0.025)		
Week 10, n=376,390	-0.88 (± 0.034)	-0.96 (± 0.033)		
Week 18, n=360,365	-1.04 (± 0.038)	-1.14 (± 0.038)		
Week 26, n=345,350	-1.04 (± 0.041)	-1.1 (± 0.040)		

Notes:

[16] - FA Population.

[17] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 4.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
P-value	< 0.0001
Method	t-test, 1-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.18
upper limit	-0.07

Notes:

[18] - Difference in change from Baseline least squares means (albiglutide - insulin lispro) is greater than 0.30% based on one-sided t-test with 0.025 level of significance

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 5.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
P-value	< 0.0001
Method	t-test, 1-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	-0.02

Notes:

[19] - Difference in change from Baseline least squares means (albiglutide - insulin lispro) is greater than 0.30% based on one-sided t-test with 0.025 level of significance

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 10.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	non-inferiority[20]
P-value	< 0.0001
Method	t-test, 1-sided
Parameter estimate	Mean difference (net)
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.17

Notes:

[20] - Difference in change from Baseline least squares means (albiglutide - insulin lispro) is greater than 0.30% based on one-sided t-test with 0.025 level of significance

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 18.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine

Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	non-inferiority[21]
P-value	< 0.0001
Method	t-test, 1-sided
Parameter estimate	Mean difference (net)
Point estimate	0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.21

Notes:

[21] - Difference in change from Baseline least squares means (albiglutide - insulin lispro) is greater than 0.30% based on one-sided t-test with 0.025 level of significance

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 26.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
P-value	< 0.0001
Method	t-test, 1-sided
Parameter estimate	Mean difference (net)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.17

Notes:

[22] - Difference in change from Baseline least squares means (albiglutide - insulin lispro) is greater than 0.30% based on one-sided t-test with 0.025 level of significance

Secondary: Change from Baseline in Fasting plasma glucose (FPG) at Week 26

End point title	Change from Baseline in Fasting plasma glucose (FPG) at Week 26

End point description:

FPG was measured at Baseline (Day -1). FPG values for all participants at Week 26 were not collected due to an error in the protocol and were imputed with the fasting serum glucose (FSG) values at this time point. The imputation of the FPG at Week 26 from the FSG values was deemed acceptable from the results of the analysis of the correlation between FPG and FSG at the screening visit. The Baseline value was the last available non-missing value prior to the first dose of the randomized treatment, thus Baseline was Day -1. Change from Baseline is defined as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	345[23]	349[24]		
Units: Millimoles per Liter				
least squares mean (standard error)				
Millimoles per Liter	-2.01 (± 0.120)	-1.46 (± 0.121)		

Notes:

[23] - FA Population. Only those participants available at the specified time points were analyzed.

[24] - FA Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	694
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	-0.25

Secondary: Change from Baseline to Week 26 in FPG

End point title	Change from Baseline to Week 26 in FPG

End point description:

FPG was measured at Baseline (Day -1) up to Week 26. FPG values for all participants at Week 26 were not collected due to an error in the protocol and were imputed with the FSG values at this time point. The imputation of the FPG at Week 26 from the FSG values was deemed acceptable from the results of the analysis of the correlation between FPG and FSG at the screening visit. The Baseline value was the last available non-missing value prior to the first dose of the randomized treatment, thus Baseline was Day -1. Change from Baseline is defined as the post-Baseline value minus the Baseline value.

End point type	Secondary

End point timeframe:

Baseline to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[25]	412[26]		
Units: Millimoles per Liter				
least squares mean (standard error)				
Week 4, n=356,371	-1.30 (± 0.119)	-0.76 (± 0.118)		
Week 5, n=366,388	-1.07 (± 0.126)	-0.88 (± 0.125)		
Week 18, n=348,353	-1.76 (± 0.124)	-1.23 (± 0.124)		
Week 26, n=345,349	-2.01 (± 0.120)	-1.46 (± 0.121)		

Notes:

[25] - FA Population. Only those participants available at the specified time points were analyzed.

[26] - FA Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 4.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.84
upper limit	-0.24

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 5.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine

Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.51
upper limit	0.13

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 18.	
Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.85
upper limit	-0.22

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 26.	
Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	t-test, 2-sided
Parameter estimate	Mean difference (net)
Point estimate	-0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.86
upper limit	-0.25

Secondary: Number of participants achieving HbA1c <7.0% at Week 26

End point title	Number of participants achieving HbA1c <7.0% at Week 26

End point description:

HbA1c is glycosylated hemoglobin. Number of participants achieving a HbA1c <7.0% at Week 26 are presented.

End point type	Secondary

End point timeframe:

Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[27]	412[28]		
Units: Participants				
Participants	244	255		

Notes:

[27] - FA Population.

[28] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7026 [29]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.31

Notes:

[29] - Non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for Baseline HbA1c category, age category, region and current use of metformin.

Secondary: Number of participants achieving HbA1c <7.0% up to Week 26

End point title	Number of participants achieving HbA1c <7.0% up to Week 26

End point description:

HbA1c is glycosylated hemoglobin. Number of participants achieving a HbA1c <7.0% up to Week 26 are

presented.

End point type	Secondary

End point timeframe:

Up to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[30]	412[31]		
Units: Participants				
Week 4	142	139		
Week 5	157	182		
Week 10	220	261		
Week 18	251	281		
Week 26	244	255		

Notes:

[30] - FA Population.

[31] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 4.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2883 [32]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.64

Notes:

[32] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 5.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine

Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3034 [33]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.15

Notes:

[33] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 10.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0151 [34]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.71
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	0.98

Notes:

[34] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 18.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0518 [35]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.75

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.03

Notes:

[35] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 26.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7026 [36]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.31

Notes:

[36] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin

Secondary: Number of participants achieving a HbA1c <6.5% at Week 26

End point title	Number of participants achieving a HbA1c <6.5% at Week 26

End point description:

Number of participants achieving a HbA1c <6.5% at Week 26 are presented.

End point type	Secondary

End point timeframe:

Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[37]	412[38]		
Units: Participants				
Participants	147	169		

Notes:

[37] - FA Population.

[38] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2298 [39]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.17

Notes:

[39] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Secondary: Number of participants achieving a HbA1c <6.5% up to Week 26

End point title	Number of participants achieving a HbA1c <6.5% up to Week 26

End point description:

Number of participants achieving a HbA1c <6.5% up to Week 26 are presented.

End point type	Secondary

End point timeframe:

Up to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[40]	412[41]		
Units: Participants				
Week 4	39	33		
Week 5	63	62		
Week 10	116	140		
Week 18	150	178		
Week 26	147	169		

Notes:

[40] - FA Population.

[41] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 4.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2143 [42]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	2.23

Notes:

[42] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 5.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4703 [43]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.91

Notes:

[43] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 10.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine

Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2139 [44]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.14

Notes:

[44] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 18.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.079 [45]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	1.11

Notes:

[45] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 26.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2298 [46]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.85

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.17

Notes:

[46] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Secondary: Number of participants who met prespecified criteria for severe, persistent hyperglycemia at Week 26

End point title	Number of participants who met prespecified criteria for severe, persistent hyperglycemia at Week 26

End point description:

Meeting prespecified criteria for severe, persistent hyperglycemia was defined operationally as being withdrawn due to lack of efficacy as recorded on the Treatment Discontinuation and Study Conclusion electronic case report form pages. Number of participants who met prespecified criteria for severe, persistent hyperglycemia at Week 26 are presented.

End point type	Secondary

End point timeframe:

Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[47]	412[48]		
Units: Participants				
Participants	3	3		

Notes:

[47] - FA Population.

[48] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8292 [49]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	4.77

Notes:

[49] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Secondary: Number of participants meeting prespecified criteria for severe, persistent hyperglycemia up to Week 26

End point title	Number of participants meeting prespecified criteria for severe, persistent hyperglycemia up to Week 26

End point description:

Meeting prespecified criteria for severe, persistent hyperglycemia was defined operationally as being withdrawn due to lack of efficacy as recorded on the Treatment Discontinuation and Study Conclusion electronic case report form pages. Number of participants meeting prespecified criteria for severe, persistent hyperglycemia up to Week 26 are presented.

End point type	Secondary

End point timeframe:

Up to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[50]	412[51]		
Units: Participants				
0 to <=4 Weeks	0	0		
>4 to <=5 Weeks	0	0		
>5 to <=10 Weeks	2	0		
>10 to <=18 Weeks	0	1		
>18 to <=26 Weeks	1	2		

Notes:

[50] - FA Population.

[51] - FA Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Total daily insulin dose at Week 4, Week 10 and Week 18

End point title	Total daily insulin dose at Week 4, Week 10 and Week 18

End point description:

Based on MMRM model, prescribed total daily basal insulin dose was equal to Baseline prescribed total daily basal insulin dose + treatment + Baseline HbA1c category + region + age category + current use of metformin + visit week + treatment-by-visit week interaction + Baseline prescribed total daily basal insulin dose-by-visit week interaction. Total daily insulin dose at Week 4, Week 10 and Week 18 is presented. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles.

End point type	Secondary

End point timeframe:

Weeks 4, 10, and 18

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[52]	412[53]		
Units: International Units				
least squares mean (standard error)				
Week 4, n=388,403	50.53 (± 1.183)	106.91 (± 1.187)		
Week 10, n=375,386	57.99 (± 1.597)	121.69 (± 1.589)		
Week 18, n=359,361	68.23 (± 2.010)	130.22 (± 1.998)		

Notes:

[52] - FA Population.

[53] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 4.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-56.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.19
upper limit	-53.57

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 10.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-63.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-67.78
upper limit	-59.62

Statistical analysis title	Statistical analysis 3
Statistical analysis description: Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 18.	
Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-67.29
upper limit	-56.7

Secondary: Total daily basal insulin (insulin glargine) at Week 4, 10, 18, and 26 visits

End point title	Total daily basal insulin (insulin glargine) at Week 4, 10, 18, and 26 visits
End point description: Based on MMRM model, prescribed total daily basal insulin dose was equal to Baseline prescribed total daily basal insulin dose + treatment + Baseline HbA1c category + region + age category + current use of metformin + visit week + treatment-by-visit week interaction + Baseline prescribed total daily basal insulin dose-by-visit week interaction. Total daily basal insulin (insulin glargine) at Week 4, 10, 18, and 26 visits is presented. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles.	
End point type	Secondary
End point timeframe: Weeks 4, 10, 18, and 26	

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[54]	412[55]		
Units: International Units				
least squares mean (standard error)				
Week 4, n=388,403	49.97 (± 0.534)	50.94 (± 0.536)		
Week 10, n=375,386	56.14 (± 0.767)	55.79 (± 0.761)		
Week 18, n=359,361	59.42 (± 0.928)	59.18 (± 0.920)		
Week 26, n=342,341	59.83 (± 0.996)	59.43 (± 0.988)		

Notes:

[54] - FA Population.

[55] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 4.	
Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Mean difference (final values)
Point estimate	-0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.25
upper limit	0.3

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 10.	
Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.64
upper limit	2.33

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 18.	
Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine

Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.21
upper limit	2.69

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 26.

Comparison groups	Albiglutide + Insulin Glargine v Insulin Lispro + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7699
Method	t-Test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.25
upper limit	3.04

Secondary: Total daily bolus insulin (insulin lispro) at Week 4, 10, 18, and 26 visits

End point title	Total daily bolus insulin (insulin lispro) at Week 4, 10, 18, and 26 visits

End point description:

Based on MMRM model, prescribed total daily basal insulin dose was equal to Baseline prescribed total daily basal insulin dose + treatment + Baseline HbA1c category + region + age category + current use of metformin + visit week + treatment-by-visit week interaction + Baseline prescribed total daily basal insulin dose-by-visit week interaction. Total daily bolus insulin (insulin lispro) at Week 4, 10, 18, and 26 visits is presented. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles.

End point type	Secondary

End point timeframe:

Weeks 4, 10, 18, and 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[56]	412[57]		
Units: International Units				
least squares mean (standard error)				
Week 4, n=388,403	0.62 (± 0.887)	56.67 (± 0.892)		
Week 10, n=375,386	1.90 (± 1.147)	66.66 (± 1.144)		
Week 18, n=359,361	8.89 (± 1.436)	71.81 (± 1.430)		
Week 26, n=342,341	10.64 (± 1.523)	72.47 (± 1.517)		

Notes:

[56] - FA Population.

[57] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 4.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-56.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.17
upper limit	-53.94

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 10.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-64.76

Confidence interval	
level	95 %
sides	2-sided
lower limit	-67.68
upper limit	-61.85

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 18.	
Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (final values)
Point estimate	-62.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.69
upper limit	-59.15

Statistical analysis title	Statistical analysis 4
Statistical analysis description:	
Least square mean difference (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented for Week 26.	
Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	-61.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-65.85
upper limit	-57.81

Secondary: Total number of weekly insulin injections to achieve glycemic control at Baseline/Randomization and Week 4, 10, 18, and 26

End point title	Total number of weekly insulin injections to achieve glycemic

	control at Baseline/Randomization and Week 4, 10, 18, and 26

End point description:

Total number of weekly insulin injections (7 days) to achieve glycemic control at Baseline/Randomization and Week 4, 10, 18, and 26 are presented. Only those participants available at the specified time points were analyzed represented by n=X,X in category titles.

End point type	Secondary

End point timeframe:

Baseline (Day -1) and Weeks 4, 10, 18 and 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[58]	412[59]		
Units: Insulin Injections				
arithmetic mean (standard deviation)				
Baseline, n=401,412	28.79 (± 1.470)	28.00 (± 0.000)		
Week 4, n=388,403	8.11 (± 1.506)	28.00 (± 0.000)		
Week 10, n=375,386	9.06 (± 3.121)	28.00 (± 0.000)		
Week 18, n=359,361	12.62 (± 7.330)	28.00 (± 0.000)		
Week 26, n=342,341	13.22 (± 7.758)	28.00 (± 0.000)		

Notes:

[58] - FA Population.

[59] - FA Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving HbA1c <7.0% without weight gain at Week 26

End point title	Percentage of participants achieving HbA1c <7.0% without weight gain at Week 26

End point description:

Percentage of participants achieving HbA1c <7.0% without weight gain are presented.

End point type	Secondary

End point timeframe:

Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[60]	412[61]		
Units: Percentage of participants				
number (not applicable)				
Percentage of participants	49.8	21.4		

Notes:

[60] - FA Population.

[61] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [62]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.52
upper limit	4.86

Notes:

[62] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Secondary: Percentage of participants achieving HbA1c <7.0% without severe or documented symptomatic hypoglycemia at Week 26

End point title	Percentage of participants achieving HbA1c <7.0% without severe or documented symptomatic hypoglycemia at Week 26

End point description:

Percentage of participants achieving HbA1c <7.0% without severe or documented symptomatic hypoglycemia are presented.

End point type	Secondary

End point timeframe:

Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[63]	412[64]		
Units: Percentage of participants				
number (not applicable)				
Percentage of participants	21.1	9.5		

Notes:

[63] - FA Population.

[64] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [65]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	2.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.54
upper limit	3.6

Notes:

[65] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Secondary: Percentage of participants achieving HbA1c <7.0% without weight gain and without severe or documented hypoglycemia at Week 26

End point title	Percentage of participants achieving HbA1c <7.0% without weight gain and without severe or documented hypoglycemia at Week 26

End point description:

Percentage of participants achieving HbA1c <7.0% without weight gain and without severe or documented hypoglycemia are presented.

End point type	Secondary

End point timeframe:

Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	402[66]	412[67]		
Units: Percentage of participants				
number (not applicable)				
Percentage of participants	15.9	3.9		

Notes:

[66] - FA Population.

[67] - FA Population.

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Odds ratio (albiglutide + insulin glargine minus insulin lispro + insulin glargine) has been presented.

Comparison groups	Insulin Lispro + Insulin Glargine v Albiglutide + Insulin Glargine
Number of subjects included in analysis	814
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [68]
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	3.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.21
upper limit	6.48

Notes:

[68] - Analysis was performed using non-parametric Cochran-Mantel-Haenszel (CMH) test after adjusting for baseline HbA1c category, age category, region and current use of metformin.

Secondary: Number of participants with on-therapy adverse events (AE) and serious AE (SAE), and AE leading to discontinuation of randomized study medication

End point title	Number of participants with on-therapy adverse events (AE) and serious AE (SAE), and AE leading to discontinuation of randomized study medication

End point description:

AE is any untoward medical occurrence in a participant, temporally associated with use of medicinal product (MP), whether or not considered related to MP. AE can be any unfavorable, unintended sign (also an abnormal laboratory finding), symptom, or disease (new/exacerbated) temporally associated with use of MP. SAE is any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability, or is a congenital anomaly/birth defect or is medically significant or all events of possible drug induced liver injury with hyperbilirubinemia. Safety Population: All participants who received at least 1 dose of randomized study medication. A participant randomized to Albiglutide + Insulin glargine by mistake received Insulin Lispro + Insulin Glargine instead. Since this participant received actual treatment as Insulin Lispro + Insulin Glargine, was summarized as such in Safety Population.

End point type	Secondary

End point timeframe:

Up to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[69]	413[70]		
Units: Participants				
AE	261	254		
SAE	23	31		
AE leading to study medication discontinuation	12	6		

Notes:

[69] - Safety Population.

[70] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with other AE of special interest

End point title	Number of participants with other AE of special interest

End point description:

AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with use of a MP, whether or not considered related to MP. AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with use of MP. AE of special interest included hypoglycemic events, cardiovascular events, gastrointestinal events, injection site reactions, potential systemic allergic reactions, pancreatitis, pancreatic cancer, malignant neoplasms following treatment with insulin, diabetic retinopathy events, appendicitis, liver events, pneumonia, and atrial fibrillation/flutter.

End point type	Secondary

End point timeframe:

Up to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[71]	413[72]		
Units: Participants				
Hypoglycemic Events	305	361		
Cardiovascular Events	7	9		
Gastrointestinal Events	102	53		
Injection Site Reactions	8	1		
Systemic Allergic Reactions	3	0		
Pancreatitis	1	0		
Pancreatic cancer	0	0		
Malignant Neoplasm	2	2		
Diabetic Retinopathy	4	17		
Appendicitis	1	0		

Liver Events	0	2		
Pneumonia	1	3		
Atrial Fibrillation/Flutter	4	1		

Notes:

[71] - Safety Population.

[72] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with events of hypoglycemia with confirmed home blood glucose monitoring and/or third-party intervention through Week 26

End point title	Percentage of participants with events of hypoglycemia with confirmed home blood glucose monitoring and/or third-party intervention through Week 26

End point description:

Hypoglycemic events with confirmed home plasma glucose monitoring <3.9 millimoles per Liter and/or requiring third party intervention were severe, documented symptomatic (DS) and asymptomatic hypoglycemic events. Participants with more than one hypoglycemic event are counted in all categories reported. Any severe, documented symptomatic, and asymptomatic hypoglycemic events in 3-month intervals (i.e., from Day 0 to Week 12, >Week 12 to Week 26) are presented.

End point type	Secondary

End point timeframe:

Up to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400	413		
Units: Percentage of participants				
number (not applicable)				
Any event: Onset date falls under 0 to <= 12 weeks	55.3	79.2		
Any event: Onset date falls > 12 to <= 26 Weeks	60.3	79.4		
Severe: Onset date falls under 0 to <= 12 weeks	1.8	3.6		
Severe: Onset date falls > 12 to <= 26 Weeks	0.8	1.9		
DS: Onset date falls under 0 to <= 12 weeks	33.8	63.0		
DS: Onset date falls > 12 to <= 26 Weeks	40.8	62.0		
Asymptomatic: Onset date under 0 to <= 12 weeks	38.3	56.9		
Asymptomatic: Onset date falls > 12 to <= 26 Weeks	44.3	54.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with hypoglycemic events (in total and by each category as defined by the American Diabetes Association criteria)

End point title	Number of participants with hypoglycemic events (in total and by each category as defined by the American Diabetes Association criteria)

End point description:

The American Diabetes Association has categorized hypoglycemic events as follows: Severe, documented symptomatic, asymptomatic, probably symptomatic and pseudohypoglycemia. Number of participants with hypoglycemic events in total are also presented.

End point type	Secondary

End point timeframe:

Up to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[73]	413[74]		
Units: Participants				
Severe	9	22		
Documented Symptomatic	203	299		
Asymptomatic	230	293		
Probably Symptomatic	29	52		
Pseudohypoglycemia	45	83		
Missing	9	13		
Total	305	361		

Notes:

[73] - Safety Population.

[74] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with daytime and nocturnal hypoglycemia

End point title	Number of participants with daytime and nocturnal hypoglycemia

End point description:

Daytime hypoglycemia was defined as hypoglycemic events with an onset between 06:00 hours and 00:00 hours (inclusive), and nocturnal hypoglycemia (in total and by category), defined as hypoglycemic events with an onset between 00:01 hours and 05:59 hours (inclusive). Number of participants with daytime and nocturnal hypoglycemia (in total and by category) are presented.

End point type	Secondary

End point timeframe:

Up to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[75]	413[76]		
Units: Participants				
Any (Total) Daytime Hypoglycemic Event	288	356		
Any (Total) Nocturnal Hypoglycemic Event	155	225		
Severe Daytime Hypoglycemic Event	6	14		
Severe Nocturnal Hypoglycemic Event	4	6		
Documented Symptomatic Daytime Hypoglycemic event	187	293		
Documented Symptomatic Nocturnal Hypoglycemia	101	152		
Asymptomatic Daytime Hypoglycemic event	217	281		
Asymptomatic Nocturnal Hypoglycemic event	77	106		
Probably Symptomatic Daytime Hypoglycemic event	22	4		
Probably Symptomatic Nocturnal Hypoglycemic event	7	21		
Pseudohypoglycemia Daytime Hypoglycemic event	36	70		
Pseudohypoglycemia Nocturnal Hypoglycemic event	17	34		
Missing Daytime Hypoglycemic Event	9	11		
Mising Nocturnal Hypoglycemic Event	2	4		

Notes:

[75] - Safety Population.

[76] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with hypoglycemia with blood glucose <56 milligrams per deciliter (mg/dL) (<3.1 millimoles per liter [mmol/L]), regardless of symptoms

End point title	Number of participants with hypoglycemia with blood glucose <56 milligrams per deciliter (mg/dL) (<3.1 millimoles per liter [mmol/L]), regardless of symptoms

End point description:

Number of participants with hypoglycemia with blood glucose <56 mg/dL (<3.1 mmol/L), regardless of symptoms are presented.

End point type	Secondary

End point timeframe:

Up to Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[77]	413[78]		
Units: Participants				
Participants	141	239		

Notes:

[77] - Safety Population.

[78] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with hematology values of clinical concern

End point title	Number of participants with hematology values of clinical concern

End point description:

Hematology parameters included basophils, eosinophils, hematocrit, hemoglobin, lymphocytes, monocytes, neutrophils, neutrophil bands, platelets, red blood cell (RBC) count, segmented neutrophils and white blood cell (WBC) count. The potential clinical concern values were: Hematocrit >0.05 below lower limit of normal (LLN) and >0.04 above upper limit of normal (ULN), hemoglobin: >20 grams cells per Liter (g/L) below LLN and >10 g/L above ULN, lymphocytes: <0.5 x LLN, neutrophils: <1 giga cells per liter (GI/L), platelets: <80 GI/L and >500 GI/L, segmented neutrophils: <0.5 x LLN, RBC count: >1 GI/L below LLN and >5 GI/L above ULN and none for basophils, eosinophils, monocytes, neutrophil bands and RBC count. Only those parameters for which at least one value of potential clinical concern was reported are summarized.

End point type	Secondary

End point timeframe:

Up to 30 weeks

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	394[79]	407[80]		
Units: Participants				
Hematocrit: >0.05 (fraction) below LLN	5	6		
Hematocrit: >0.04 (fraction) above ULN	9	12		
Hemoglobin: >20 g/L below LLN	9	9		
Hemoglobin: >10 g/L above ULN	2	3		
Leukocytes: >1 GI/L below LLN	1	1		
Leukocytes: >5 GI/L above ULN	4	1		
Neutrophils: <1 GI/L	2	3		
Neutrophils, Segmented: <0.5 x LLN	2	3		
Platelets: <80 GI/L	1	1		
Platelets: >500 GI/L	3	1		

Notes:

[79] - Safety Population. Only those participants available at the specified time points were analyzed.

[80] - Safety Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinical chemistry values of clinical concern

End point title	Number of participants with clinical chemistry values of clinical concern

End point description:

Clinical chemistry parameters and their potential clinical concern values were: albumin (>5 g/L above ULN or below LLN), alkaline phosphatase(>3 x ULN), alanine aminotransferase (>3 x ULN), aspartate aminotransferase (>3 x ULN), carbon dioxide content (<16 millimoles per Liter [mmol/L] and > 40 mmol/L), blood urea nitrogen (>2 x ULN), calcium (<1.8 mmol/L and >3.0 mmol/L), chloride (none), creatinine (>159 micromoles/Liter), direct bilirubin (>1.35 x ULN), gamma glutamyl transferase (>3 x ULN), glucose (fasting) (<3 mmol/L and >22 mmol/L), magnesium (<0.411 mmol/L and >1.644 mmol/L), phosphate (>0.323 mmol/L above ULN or below LLN), potassium (>0.5 mmol/L below LLN and >1.0 mmol/L above ULN), sodium (>5 mmol/L above ULN or below LLN), triglycerides (> 9.04 mmol/L), total bilirubin (>1.5 x ULN), total protein (>15 g/L above ULN or below LLN) and uric acid (>654 umol/L). Only those parameters for which at least one value of potential clinical concern was reported are summarized.

End point type	Secondary

End point timeframe:

Up to 30 weeks

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[81]	413[82]		
Units: Participants				
Fasting Serum Glucose: <3 mmol/L, n= 394,405	12	16		
Fasting Serum Glucose: >22 mmol/L, n= 394,405	0	1		
Fasting Plasma Glucose: <3 mmol/L, n= 388,406	9	14		
Fasting Plasma Glucose: >22 mmol/L, n= 388,406	1	0		
Albumin: >5 g/L below LLN, n=394,407	0	0		
Albumin: >5 g/L above ULN, n=394,407	0	0		
Calcium: <1.8 mmol/L, n=394,407	1	1		
Calcium: >3.0 mmol/L, n=394,407	0	0		
Carbon Dioxide: <16 mmol/L, n=394,407	5	8		
Carbon Dioxide: >40 mmol/L, n=394,407	0	0		
Magnesium: <0.411 mmol/L, n=394,407	1	1		
Magnesium: >1.644 mmol/L, n=394,407	0	0		
Phosphate: >0.323 mmol/L below LLN, n=394,407	0	0		
Phosphate: >0.323 mmol/L above ULN, n=394,407	2	4		
Potassium: >0.5 mmol/L below LLN, n=394,407	1	0		
Potassium: >1.0 mmol/L above ULN, n=394,407	0	1		

Protein: >15 g/L below LLN, n=394,407	0	0		
Protein: >15 g/L above ULN, n=394,407	0	0		
Sodium: >5 mmol/L below LLN, n=394,407	1	0		
Sodium: >5 mmol/L above ULN, n=394,407	1	0		
Triglycerides: >9.04 mmol/L, n=393,405	7	1		
Urate: >654 µmol/L, n=394,407	0	2		
Urea: >2 x ULN, n=394,407	2	1		
Alanine Aminotransferase: >3 x ULN, n=396,410	0	5		
Alkaline Phosphatase: >3 x ULN, n=396,410	1	0		
Aspartate Aminotransferase: >3 x ULN, n=396,410	0	2		
Bilirubin: >1.5 x ULN, n=396,410	1	1		
Creatinine: >159 µmol/L, n=396,410	20	16		
Direct Bilirubin: >1.35 x ULN, n=396,410	0	1		
Gamma Glutamyl Transferase: >3 x ULN, n=396,410	14	14		

Notes:

[81] - Safety Population. Only those participants available at the specified time points were analyzed.

[82] - Safety Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean urine albumin/creatinine ratio at Week 0 and Week 26

End point title	Mean urine albumin/creatinine ratio at Week 0 and Week 26

End point description:

Urine samples were collected for analysis of albumin/creatinine ratio. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles. Mean urine albumin/creatinine ratio at Week 0 and Week 26 are presented.

End point type	Secondary

End point timeframe:

Week 0 and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[83]	413[84]		
Units: Grams per mole				
arithmetic mean (standard deviation)				
Week 0, n=369,376	14.40 (± 49.884)	11.57 (± 31.089)		
Week 26, n=317,324	10.37 (± 32.992)	11.55 (± 31.975)		

Notes:

[83] - Safety Population.

[84] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean albumin at Week 0 and Week 26

End point title	Mean albumin at Week 0 and Week 26

End point description:

Urine samples were collected for analysis of albumin. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles. Mean albumin at Week 0 and Week 26 are presented.

End point type	Secondary

End point timeframe:

Week 0 and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[85]	413[86]		
Units: Milligrams per Liter				
arithmetic mean (standard deviation)				
Week 0, n=394,405	127.7 (± 428.46)	108.2 (± 301.88)		
Week 26, n=348,345	110.5 (± 375.41)	146.3 (± 628.73)		

Notes:

[85] - Safety Population.

[86] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean creatinine at Week 0 and Week 26

End point title	Mean creatinine at Week 0 and Week 26

End point description:

Urine samples were collected for analysis of creatinine. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles. Mean creatinine at Week 0 and Week 26 are presented.

End point type	Secondary

End point timeframe:

Week 0 and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[87]	413[88]		
Units: Micromoles per Liter				
arithmetic mean (standard deviation)				
Week 0, n=395,406	10646.3 (± 5190.43)	10663.8 (± 5639.54)		
Week 26, n=350,345	11364.6 (± 5998.72)	11394.2 (± 5663.72)		

Notes:

[87] - Safety Population.

[88] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean specific gravity at Week 0 and Week 26

End point title	Mean specific gravity at Week 0 and Week 26

End point description:

Urine specific gravity is a measure of the concentration of solutes in the urine and provides information on the kidney’s ability to concentrate urine. The concentration of the excreted molecules determines the urine's specific gravity. A urinary specific gravity measurement is a routine part of urinalysis. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles.

End point type	Secondary

End point timeframe:

Week 0 and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[89]	413[90]		
Units: Ratio				
arithmetic mean (standard deviation)				
Week 0, n=388,402	1.0182 (± 0.00599)	1.0180 (± 0.00588)		
Week 26, n=347,343	1.0180 (± 0.00627)	1.0186 (± 0.00588)		

Notes:

[89] - Safety Population.

[90] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with different values of potential of hydrogen (pH) at Week 0 and Week 26

End point title	Number of participants with different values of potential of hydrogen (pH) at Week 0 and Week 26

End point description:

Urine pH is an acid-base measurement. pH is measured on a numeric scale ranging from 0 to 14; values on the scale refer to the degree of alkalinity or acidity. A pH of 7 is neutral. A pH less than 7 is acidic, and a pH greater than 7 is basic. Normal urine has a slightly acid pH (5.0 - 6.0). Safety Population was analyzed. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles.

End point type	Secondary

End point timeframe:

Week 0 and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[91]	413[92]		
Units: Participants				
pH=5; Week 0, n=388,402	92	107		
pH=5.5; Week 0, n=388,402	132	132		
pH=6; Week 0, n=388,402	86	77		
pH=6.5; Week 0, n=388,402	29	43		
pH=7; Week 0, n=388,402	29	24		
pH=7.5; Week 0, n=388,402	13	11		
pH=8; Week 0, n=388,402	6	7		
pH=8.5; Week 0, n=388,402	1	1		
pH=5; Week 26, n=347,343	80	100		
pH=5.5; Week 26, n=347,343	107	104		
pH=6; Week 26, n=347,343	69	70		
pH=6.5; Week 26, n=347,343	42	23		
pH=7; Week 26, n=347,343	19	23		
pH=7.5; Week 26, n=347,343	17	18		
pH=8; Week 26, n=347,343	7	5		
pH=8.5; Week 26, n=347,343	5	0		
pH>9; Week 26, n=347,343	1	0		

Notes:

[91] - Safety Population.

[92] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with different number of erythrocytes in urine at Week 0 and Week 26

End point title	Number of participants with different number of erythrocytes in urine at Week 0 and Week 26

End point description:

Urine samples were collected for analysis of erythrocyte count. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles. Number of participants with different number of erythrocytes in urine at Week 0 and Week 26 are presented.

End point type	Secondary

End point timeframe:

Week 0 and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[93]	413[94]		
Units: Participants				
None Seen; Week 0, n=171,187	119	101		
0 to 1; Week 0, n=171,187	34	51		
1 to 3; Week 0, n=171,187	9	14		
3 to 5; Week 0, n=171,187	3	12		
5 to 10; Week 0, n=171,187	2	4		
10 to 15; Week 0, n=171,187	0	2		
15 to 25; Week 0, n=171,187	2	1		
50 to 100; Week 0, n=171,187	0	1		
>100; Week 0, n=171,187	2	1		
None Seen; Week 26, n=166,144	98	79		
0 to 1; Week 26, n=166,144	48	36		
1 to 3; Week 26, n=166,144	8	19		
3 to 5; Week 26, n=166,144	4	3		
5 to 10; Week 26, n=166,144	4	4		
25 to 50; Week 26, n=166,144	1	2		
50 to 100; Week 26, n=166,144	2	0		
>100; Week 26, n=166,144	1	1		

Notes:

[93] - Safety Population.

[94] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with different number of leukocytes in urine at Week 0 and Week 26

End point title	Number of participants with different number of leukocytes in urine at Week 0 and Week 26

End point description:

Urine samples were collected for analysis of leukocyte count. Only those participants available at the specified time points were analyzed represented by n=X,X in the category titles. Number of participants with different number of leukocytes in urine at Week 0 and Week 26 are presented.

End point type	Secondary

End point timeframe:

Week 0 and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[95]	413[96]		
Units: Participants				
None Seen; Week 0, n=171,187	69	67		
0 to 1; Week 0, n=171,187	27	31		
1 to 3; Week 0, n=171,187	20	18		
3 to 5; Week 0, n=171,187	16	13		
5 to 10; Week 0, n=171,187	17	19		
10 to 15; Week 0, n=171,187	7	6		
15 to 25; Week 0, n=171,187	5	11		
25 to 50; Week 0, n=171,187	5	11		
50 to 100; Week 0, n=171,187	1	7		
>100; Week 0, n=171,187	4	3		
Innumerable; Week 0, n=171,187	0	1		
None Seen; Week 26, n=166,144	65	44		
0 to 1; Week 26, n=166,144	25	29		
1 to 3; Week 26, n=166,144	22	20		
3 to 5; Week 26, n=166,144	10	15		
5 to 10; Week 26, n=166,144	22	14		
10 to 15; Week 26, n=166,144	8	5		
15 to 25; Week 26, n=166,144	3	3		
20 to 50; Week 26, n=166,144	0	1		
25 to 50; Week 26, n=166,144	5	6		
50 to 100; Week 26, n=166,144	5	5		
>100; Week 26, n=166,144	1	1		
Innumerable; Week 26, n=166,144	0	1		

Notes:

[95] - Safety Population.

[96] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), high density lipoprotein (HDL-c), triglycerides (TG) and free fatty acids (FFA) at Week 10 and Week 26

End point title	Change from Baseline in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), high density lipoprotein (HDL-c), triglycerides (TG) and free fatty acids (FFA) at Week 10 and Week 26

End point description:

Lipid parameters included TC, LDL-c, HDL-c, TG and FFA. The Baseline value was the last available non-missing value prior to the first dose of the randomized treatment, thus Baseline was Day -1. Change from Baseline is defined as the post-Baseline value minus the Baseline value. LDL-c and FFA were collected as part of the lipid panel and results were reviewed by investigators for individual participants. Change from Baseline at Week 10 and Week 26 was not assessed for these parameters. Analysis of these parameters was not a specific study objective and would not have any impact on study conclusions. Only those parameters with data values have been presented. Only those participants

available at the specified time points were analyzed represented by n=X,X in the category titles.

End point type	Secondary

End point timeframe:

Baseline, Week 10 and Week 26

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	400[97]	413[98]		
Units: Millimoles per Liters				
arithmetic mean (standard deviation)				
TC: Week 10, n=376,393	-0.244 (± 0.8047)	0.041 (± 0.7425)		
TC: Week 26, n=348,351	-0.059 (± 0.8721)	0.073 (± 0.8232)		
HDL-c: Week 10, n=376,393	-0.041 (± 0.1944)	0.016 (± 0.1810)		
HDL-c: Week 26, n=348,351	-0.013 (± 0.2102)	0.005 (± 0.2138)		
TG: Week 10, n=376,393	-0.039 (± 1.3563)	-0.065 (± 0.8045)		
TG: Week 26, n=348,351	0.025 (± 1.1949)	-0.028 (± 0.9342)		

Notes:

[97] - Safety Population.

[98] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with vital signs of clinical concern

End point title	Number of participants with vital signs of clinical concern

End point description:

Vital signs included systolic blood pressure (SBP), diastolic blood pressure (DBP) and pulse rate values. Assessment of vitals were performed with the participant in a semi recumbent or seated position having rested in this position for at least 5 minutes before each reading. The potential clinical concern values were: SBP: <100 millimeters of mercury (mmHg) and >170 mmHg, DBP: <50 mmHg and >110 mmHg and pulse rate: <50 beats per minute (bpm) and > 120 bpm. Number of participants with vital signs of clinical concern are presented.

End point type	Secondary

End point timeframe:

Up to 30 weeks

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	397[99]	411[100]		
Units: Participants				
SBP: < 100 mmHg	21	20		
SBP: > 170 mmHg	27	30		
DBP: < 50 mmHg	1	4		
DBP: > 110 mmHg	1	5		
Pulse Rate: < 50 bpm	4	9		
Pulse Rate: > 120 bpm	3	1		

Notes:

[99] - Safety Population. Only those participants available at the specified time points were analyzed.

[100] - Safety Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically significant change in electrocardiogram (ECG) parameters

End point title	Number of participants with clinically significant change in electrocardiogram (ECG) parameters

End point description:

A single 12-lead ECG recordings were performed in a participant in semi recumbent position for 10 to 15 minutes before obtaining the ECG. Any clinically significant favorable and unfavorable findings are reported.

End point type	Secondary

End point timeframe:

Up to 30 weeks

End point values	Albiglutide + Insulin Glargine	Insulin Lispro + Insulin Glargine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	384[101]	394[102]		
Units: Participants				
Clinically Significant Change: Favorable	18	9		
Clinically Significant Change: Unfavorable	4	5		

Notes:

[101] - Safety Population. Only those participants available at the specified time points were analyzed.

[102] - Safety Population. Only those participants available at the specified time points were analyzed.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 26 weeks

Adverse event reporting additional description:

On-therapy SAE and non-serious AE were collected for Safety Population which comprised of all participants who receive at least 1 dose of randomized study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Insulin Lispro + Insulin Glargine

Reporting group description:

During standardization period, participants transitioned from basal bolus regimen received during screening period to insulin glargine plus insulin lispro. Eligible participants continued with the same doses as at the end of the standardization period and doses were adjusted according to protocol-defined insulin titration algorithms. Participants received Insulin Glargine along with Insulin Lispro during the treatment period.

Reporting group title	Albiglutide + Insulin Glargine

Reporting group description:

During standardization period, participants transitioned from basal bolus regimen received during screening period to insulin glargine plus insulin lispro. Eligible participants received Albiglutide 30 mg weekly SC injection during the treatment period and insulin lispro dose was down-titrated to half that used in the standardization period. At Week 4, Albiglutide was up-titrated to 50 mg weekly SC injection and insulin lispro was stopped for the remainder of the treatment period.

Serious adverse events	Insulin Lispro + Insulin Glargine	Albiglutide + Insulin Glargine	
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 413 (7.51%)	23 / 400 (5.75%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Teratoma			

subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral ischaemia			
subjects affected / exposed	1 / 413 (0.24%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Reproductive system and breast disorders			
Metrorrhagia			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ligament injury			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal injury			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	2 / 413 (0.48%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	1 / 413 (0.24%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 413 (0.24%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem infarction			

subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperaesthesia			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Conductive deafness			

subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mesenteric artery stenosis			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 413 (0.48%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	2 / 413 (0.48%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 413 (0.00%)	1 / 400 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypoglycaemia			

subjects affected / exposed	6 / 413 (1.45%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	6 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 413 (0.24%)	0 / 400 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Insulin Lispro + Insulin Glargine	Albiglutide + Insulin Glargine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	101 / 413 (24.46%)	114 / 400 (28.50%)	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	18 / 413 (4.36%)	31 / 400 (7.75%)	
occurrences (all)	19	51	
Nausea			
subjects affected / exposed	7 / 413 (1.69%)	37 / 400 (9.25%)	
occurrences (all)	7	53	
Infections and infestations			
Influenza			
subjects affected / exposed	36 / 413 (8.72%)	24 / 400 (6.00%)	
occurrences (all)	42	30	
Viral upper respiratory tract infection			
subjects affected / exposed	34 / 413 (8.23%)	25 / 400 (6.25%)	
occurrences (all)	39	33	
Urinary tract infection			
subjects affected / exposed	23 / 413 (5.57%)	22 / 400 (5.50%)	
occurrences (all)	24	25	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 June 2015	Amendment No. 1: Clarify potentially confusing text. Add details of sensitivity analyses that will assess the impact of missing data for the noninferiority test. Introduce additional flexibility into glycemic eligibility criteria at Screening and to the process for transitioning participants from their prior basal-bolus insulin therapy to insulin glargine and insulin lispro at the beginning of the Standardization Period, as well as provide additional flexibility to the investigator when adjusting insulin glargine and insulin lispro. Further mitigate the potential risk of hypoglycemia, as well as enhance participants education and training pertaining to hypoglycemic events. Add an optional fasting glycosylated hemoglobin (HbA1c) test at Screening to aid investigators in the selection of participants who may be good candidates for the study. Add a stimulated C-peptide assessment at Screening as a complimentary assessment for participants to demonstrate reserve insulin secretory capacity. Incorporate other administrative changes.
10 June 2015	Amendment No. 2: The inclusion criterion pertaining to adequate contraception was updated to indicate that progestogen-only pills are only acceptable if they have a Pearl Index of less than 1.0. A criterion was added to exclude persons who have been put in an institution because of official or legal order. A criterion was added to exclude employees (or the employee's relatives) of the sponsor, the contract research organization, or the investigative site.
24 September 2015	Amendment No. 3: Correct International System of units (SI units) for select blood glucose concentrations millimole per liter (mmol/L) for insulin titration. Combine global amendment 01 and country-specific amendments into a single protocol document. To aid clarity, country-specific requirements have been clearly identified. Incorporate other administrative changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported